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Estimated burden of serious fungal infections in Togo

Ameyo M. Dorkenoo[1,2] | Akovi K. Adjetey-Toglozombio[1] | Bright K. Ocansey[3] | Efoe Sossou[2] | Fiali Lack[2] | David W. Denning[3]

[1]Département de Parasitologie-Mycologie, Faculté des Sciences de la Santé, Université de Lomé, Lomé, Togo

[2]Ministère de la Santé et de l'Hygiène Publique, Lomé, Togo

[3]Division of Infection, Immunity and Respiratory Medicine, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

Correspondence
Dorkenoo Ameyo Monique. Faculté des Sciences de la Santé, Université de Lomé, BP Togo.
Email: monicadork@yahoo.fr

Abstract

Background: Over the years, the focus of infectious diseases in many African countries has been mainly on viral, bacterial and parasitic infections. Serious fungal infections (SFIs) with comparable morbidity rate in these countries remain neglected.

Objectives: To estimate the burden of SFI in Togo and to stimulate efforts for improved attention.

Methods: Literature was thoroughly searched for epidemiological data on SFI in Togo. Incidence and/or prevalence of SFI was estimated using socio-demographics, health system's information, risk-groups data and SFI rates obtained from national and international studies.

Results: About 5.29% of the 7,265,286 Togolese population is estimated to suffer from SFI annually. Among HIV patients, 1,342, 1,650 and 330 may develop cryptococcal meningitis, *Pneumocystis* pneumonia and disseminated histoplasmosis respectively per year. Oral and oesophageal candidiasis may annually affect 19,800 and 7,535 persons, respectively, living with HIV. Estimated incidence of invasive aspergillosis (IA) was 283 cases. Prevalence of chronic pulmonary aspergillosis (CPA) was estimated at 191 cases. The annual incidence of allergic bronchopulmonary aspergillosis (ABPA) and severe asthma with fungal sensitization (SAFS) was 4,577 and 6,042 cases, respectively. Tinea capitis and recurrent *Candida* vaginitis presumably affect 232,271 children and 108,979 women respectively. Candidaemia incidence is estimated at 5 cases per 100, 000 inhabitants and fungal keratitis may affect 981 persons annually.

Conclusions: SFIs in Togo are probably more significant than expected. These findings underscore the need to increase awareness among healthcare professionals, enhance diagnostic and therapeutic capacities and intensify epidemiological studies for effective management of fungal infections in Togo.

KEYWORDS
aspergillosis, candidiasis, HIV, serious fungal infections, Togo, tuberculosis

1 | INTRODUCTION

Togo is a West African country bordered by Ghana, Benin, and Burkina Faso and has a coastline on the Atlantic Ocean to the south. The country enjoys a tropical climate on an area of 56,600 km^2 with a density of 170 km^2. The illiteracy rate is 60% and the gross domestic product (GDP) per capita is 586.3 USD.[1] Public healthcare institutions are organised into three levels comprising 515 peripheral care units, 26 district hospitals, 6 regional hospitals, 3 intermediate-level hospitals and 3 university hospitals (CHU).

Ameyo M. Dorkenoo and Akovi K. Adjetey-Toglozombio are Co-first authors.

Like most African countries, there is insufficient awareness of serious fungal infections (SFIs), particularly invasive fungal infections among healthcare workers and relevant stakeholders. In view of this, there is inadequate clinical mycology infrastructure and lack of targeted training of experts in diagnosis and management of fungal infections resulting in low index of suspicion. Meanwhile, patients suffering from HIV/AIDS, pulmonary tuberculosis (PTB), diabetes, cancer and asthma are at risk for several SFI. Presently, there is no nationwide data available on fungal infections in Togo. To obtain a national perspective and a measure of the burden, an estimate of prevalence and incidence of major SFI are required. The aim of this study was to estimate the prevalence and/or incidence of SFI in Togo and to stimulate efforts to increase attention.

2 | MATERIAL AND METHODS

Epidemiological data on SFI in Togo preceding August 2019 were obtained by a thorough online search using PubMed, Google Scholar and African Journals Online as well as grey literature. The following keywords either alone or combined were used: fungi, opportunistic fungal infections, candidiasis, cryptococcosis, fungal keratitis, aspergillosis, histoplasmosis and Togo. General population data were obtained from the Government Statistical Service.[2] Data on risk group for SFI including those suffering from asthma, HIV/AIDS, PTB, other respiratory diseases, diabetes, haematological cancers, critical care and post-surgical complication were extracted from reports from national and international institutions or agencies.[3-5] The prevalence and incidence of SFI were calculated using general or risk-group data and their corresponding assumptions based on rates from Togo or adopted rates as employed in previous SFI estimate studies. No specific ethical approval was required as the study involved analysis of previously published databases.

3 | RESULTS

3.1 | Togo's General and risk group population details

The general population estimate was 7,265,286 inhabitants in 2017 with 1,671,000 aged from 5 to 14 while women of reproductive age were 1,816,300. There were 110,000 people living with HIV/AIDS in 2017 of whom 57% were on antiretroviral (ARV) treatment. AIDS deaths in 2017 were 4700.[2] The estimated number of HIV/AIDS patients with CD4 <200/μL is 22,000.[3] In 2017, there were 2848 cases of PTB recorded in Togo.[5] Presumed asthma prevalence in adults is 183,085.[6] Estimates obtained for acute myeloid leukaemia (AML), non-AML and lung cancer were 89,499 and 76, respectively.[7,8] The total hospital beds in public health care facilities are 6,175. Number of patients under critical care were assumed to correspond to ICU beds and calculated as five percent of total hospital beds.[9] Annual chronic obstructive pulmonary disease (COPD) admissions were 4357[10] (Table 1).

3.2 | Assumptions used in estimation of SFI

Cryptococcal meningitis (CM) was assumed to occur in 6.12% of HIV patients with CD4 <200/μL while 15% developed *Pneumocystis* pneumonia.[4,11] For histoplasmosis, 1.5% HIV patients with CD4 <200/μL presumed to develop the disease annually over two years excluding African histoplasmosis albeit significantly diagnosed in Togo.[12,13] Oral candidiasis was assumed to affect 90% of new HIV patients and oesophageal candidiasis was estimated in 20% new HIV infections and in 0.5% of those receiving ARV therapy.[2,14] Chronic pulmonary aspergillosis (CPA) was estimated among PTB survivors, with about 90% surviving a year after diagnosis. Using an assumption from a Ugandan study, the incidence post-PTB was calculated as PTB with cavities (22%) × incidence of CPA in cavities (6.5%) + PTB without cavities (78%) × CPA incidence (0.2%).[5,15] The 5-year prevalence was calculated using a 15% annual death[16,17] or surgical resection rate leading to the annual prevalence of CPA in TB. The overall prevalence of CPA was obtained by assuming that 67% of cases occur after TB and 33% of cases are related to other underlying diseases such as emphysema, sarcoidosis, pneumothorax and asthma.[16-18] The prevalence of ABPA was estimated assuming 2.5% of adult patients with asthma develop ABPA while SAFS was calculated at 33% of 10% adult asthmatics.[18,19] Invasive aspergillosis (IA) was presumed to complicate several conditions; 10% of AML and an equivalent number in non-AML haematological conditions, 2.6% of lung cancer patients, 1.3% of COPD patients admitted to hospital and 4% of AIDS-related deaths.[20] An international annual incidence of 5 (3.5 in cancer and other immunocompromised conditions, 1.5 in ICU and post-major surgery) per 100, 000 inhabitants was used in estimating candidaemia.[21] The incidence of *Candida* peritonitis was estimated to be half of candidaemia occurring in critical care and after major surgery.[22] Mucormycosis prevalence was calculated with the assumption that 0.6/1,000,000 of the general population may be affected.[23] Recurrent *Candida* vaginitis was estimated with a general rate of 6% among women of reproductive.[24,25] Fungal keratitis was assumed to occur at a derived crude rate of 13.5/100,000 while tinea capitis occurred in 13.9% of schoolchildren.[26,27] Few cases of fungal neglected tropical diseases (FNTDs) such as basidiobolomycosis and mycetoma have been reported in Togo and their annual incidences were extrapolated from two single-centre retrospective studies.[28,29] However, there were no data available for sporotrichosis, conidiobolomycosis or chromoblastomycosis in Togo (Table 1).

3.3 | Estimated incidence and/or prevalence of SFI

Oral and oesophageal candidiasis had an annual incidence of 19,800 and 7,535 cases, respectively. *Pneumocystis* pneumonia, CM and disseminated histoplasmosis had incidences of 1,650, 1,342 and 330

TABLE 1 Summary of data and assumptions used in the calculation of prevalence and incidence

General population data		
Total =7,265,286; % of children =40; % of females =51; Adults =4,359,712; Number of children 5 to 14 years old (school going age) = 1,671,016 (23%); Number of women from 15 to 49 years old (reproductive age) = 1,816,322[1]		
Fungal infection	Risk-group population	Rate
HIV/AIDS condition		
Cryptococcal Meningitis	HIV/AIDS patients with CD4 <200/ul (22,000)[4]	6.12%[4]
Pneumocystis Pneumonia	HIV/AIDS patients with CD4 <200/µl (22,000)[4]	15%[11]
Histoplasmosis	HIV/AIDS patients with CD4 <200/ul (22,000)[4]	1.50%[12]
Oral candidiasis	New HIV patients (4,900)[2]	90% [52]
Oesophageal Candidiasis	New HIV patients (4,900) and ARV recipients (62,700)	20% of new HIV/AIDS patients and 5.0% of those on ARVs[14,53]
Respiratory Disease condition		
Chronic pulmonary aspergillosis, post TB	PTB (2848)[5]	PTB with cavities (22%) x rate of CPA in cavities (6.5%) + PTB without cavities (78%) x rate of CPA without cavities (0.2%)[15]
Chronic pulmonary aspergillosis, all	Occur in patients after TB[25] patients with other respiratory conditions such asthma, sarcoidosis, pneumothorax	67% [54] 33%[54]
Allergic bronchopulmonary aspergillosis	Adult asthmatics (183,085)[6]	2.5%[19]
Severe asthma with fungal sensitization	Adult asthmatics with severe asthma (18,309)[18]	33%[18]
Multiple underlying conditions		
Invasive Aspergillosis Cancer +immunocompromised conditions Respiratory disease conditions AIDS	AML (89) non-AML (499)[9] Lung cancer (76)[7] COPD annual admissions (4357)[8] AIDS deaths in 2017 (4700)[2]	10% AML +equal number for non-AML haematological malignancies[20] 2.60% lung cancer patients[20] +1.30% COPD annual admissions[20] 4% of AIDS deaths[55]
Candidaemia *Candida* peritonitis	Cancer, immunocompromised conditions, critical care, post-surgery Critical care, post-surgery	5/100,000[21] 0.75/100,000[22]
No Underlying Disease		
Mucormycosis	General population (7,265,286)[1]	0.6/1,000,000 of general population[23]
Recurrent *Candida* vaginitis (>4x/year)	Women at reproductive age (1,816,322)[1]	6%[24,25]
Fungal keratitis	General population (7, 265,286)[1]	13.5 per 100,000 persons[26]
Tinea capitis	Children aged 5-14 (167,106)[1]	13.9%[27]
Neglected tropical fungal diseases		
Basidiobolomycosis	General population (7,265,286)	Annual cases/general population[29]
Mycetoma	General population (7,265,286)	Annual cases/ general population [56]
Sporothricosis	ND	
Chromoblastomycosis	ND	

Note: ND: Not determined.

cases per year accordingly. The incidence and prevalence of CPA post-PTB were estimated at 41 cases and 128 cases, respectively. The overall prevalence of CPA is conservatively estimated at 191 patients. A prevalence of 4,577 and 6,042 cases were generated for ABPA and SAFS, respectively. The total annual incidence of IA was 283. Candidaemia has an annual incidence of 363 of which 70% (254) were in general wards with cancer and other immunocompromised conditions, and 30% (109) were in ICU and post-major surgery. *Candida* peritonitis has an estimated incidence of 54 cases. Mucormycosis is estimated to affect very few patients with an annual incidence of 4 cases. Recurrent *Candida* vaginitis was estimated to affect 108,979 women. Fungal keratitis was estimated at 981 cases per year while 232,271 schoolchildren were affected by tinea capitis annually. Basidiobolomycosis and mycetoma appear to be extremely rare with an annual incidence of 4.3 and 1.3 cases, respectively (Table 2).

TABLE 2 Estimates of the burden of serious fungal infections in Togo

Fungal infections	Prevalence	Annual incidence	Rate/100,000
HIV/AIDS condition			
Cryptococcal meningitis		1,342	18.52
Pneumocystis pneumonia		1,650	22.71
Histoplasmosis		330	4.50
Oral candidiasis		19,800	273
Oesophageal candidiasis		7,535	104
Respiratory Diseases condition			
Chronic pulmonary aspergillosis, post TB	128		1.8
Chronic pulmonary aspergillosis, all	191		3
Allergic bronchopulmonary aspergillosis	4,577		63
Severe asthma with fungal sensitization	6,042		83.2
Critical Care +Post Surgery condition			
Candida peritonitis		54	0.75
No Underlying Disease			
Recurrent Candida Vaginitis		108,979	1,500
Fungal keratitis		981	13.5
Tinea capitis	232,271		3,197
Mucormycosis	4		0.69
Basidiobolomycosis		4.3	0.06
Mycetoma		1.3	0.02
Multiple underlying conditions			
Invasive aspergillosis			
HIV/AIDS		188	
Respiratory diseases		57	3.89
Cancer +immunocompromised		38	
Candidaemia			
Cancer +immunocompromised.		254	
Critical care +Post Surgery		109	5.00
Total serious fungal infection burden (prevalence + incidence) = 384,404 5.29% of the Togolese population			

4 | DISCUSSION

The estimated rate of SFIs of 5.29% is not much different from that previously reported in Ghana (4%) and Burkina Faso (7.51%).[30,31] However, Togo's rate is higher than the rate estimated in Tanzania (3%), but far less than that revealed in Senegal (12.5%).[32,33] SFI in the Togolese population is dominated by tinea capitis and mucosal candidiasis. This is a common pattern in many sub-Saharan African (SSA) countries.[30-33] SFI were estimated in 30,849 PLWHIV of which CM accounted for 4.38%. This is slightly lower than rates from other SSA countries.[30,33-35] In Namibia and Cote d'Ivoire, the CM rate obtained by India ink, cryptococcal antigen (CrAg) testing or culture was lower than that obtained by using assumptions due to sampling method used in the studies.[36,37]The estimated rate of *Pneumocystis* pneumonia among PLWHIV was 2.67%, which is lower than rates from Ghana, Burkina Faso, Senegal and Namibia.[30-32,34] Probably, this is due to different rates employed.[33] Additionally, *Pneumocystis* pneumonia has been previously associated with GDP with majority of African countries having challenges diagnosing *Pneumocystis* pneumonia.[38] Regarding histoplasmosis, the annual incidence is 330 cases but local data were unavailable. This may possibly be an underestimation since only HIV/AIDS patients were considered and African histoplasmosis excluded. Furthermore, the majority of the patients with histoplasmosis particularly African histoplasmosis reside in rural areas where the health infrastructure is poor.[13,39,40] The incidence rates reported for oral and oesophageal candidiasis in Togo are underappreciated compared to findings of a prospective multicentre survey carried out in West Africa, which obtained a rate of 6.7 cases for oral candidiasis and 3 cases for oesophageal candidiasis per 100 patients with HIV.[41] A study on vaginal candidiasis in Togo revealed that 42.5% are caused by non-*albicans* strains, which were mostly resistant to commonly available antifungal drugs.[42] This is a significant contributory factor to the occurrence of recurrent *Candida*

vaginitis. The incidence rate estimated for fungal keratitis is significant and highlights the need for an active epidemiological study in Togo. The tinea capitis prevalence estimated is concordant with a previously reported rate among Togolese schoolchildren that ranged between 11% (in the north) and 20% (in the south).[43]

A few cases of basidiobolomycosis have been reported with an incidence rate estimated between 0.4 and 4.3 cases annually in Togo.[29,44] This is similar to the range between 1 and 4 cases found in Côte d'Ivoire, Benin and in Ghana and also consistent with the global annual incidence of 4.5 cases.[45-48] The annual incidence of mycetoma (1.3 cases) although extrapolated from a single-centre experience was very low but similar to studies in Nigeria.[49,50] However, in a similar single-centre survey in Senegal, there were 113 cases in 2 years.[51] Although prevalence rates were estimated for CPA, ABPA and SAFS in Togo, they are not often diagnosed and epidemiological data from Togo were missing in literature.

The major limitation of this study is the dearth of epidemiological data on SFI from Togo and thus estimates mostly dependent on data from other countries. There are very few studies conducted on SFI in Togo and mostly comprising of case reports, case series and laboratory reviews.[13,28,29,39] Besides insufficient awareness, conducting epidemiological studies on SFI in Togo is currently hampered by the lack of appropriate fungal diagnostics. Direct microscopy of dermatological samples, CSF, sputum, bronchoalveolar lavage (BAL) and tissue samples to demonstrate fungal elements is performed sporadically, depending on the availability of reagents. Histopathology and fungal culture including blood culture to identify fungus is not generally available and except at the university hospital laboratories. More importantly, none of the rapid tests, such as cryptococcal antigen, *Histoplasma* antigen, *Aspergillus* antigen, *Aspergillus* antibody and *Pneumocystis* PCR all listed on the WHO Essential Diagnostics List, are available in clinical settings in Togo.

5 | CONCLUSION

The estimated burden of SFI in the Togolese population was 5.29%. These prevalence and incidence rates are significant, considering the low cases reported for some major SFI in the country. This is because there is an inadequate awareness and the country is currently faced with a lack of appropriate diagnostic and therapeutic infrastructures. It is imperative to increase awareness among healthcare professionals, create and equip specialized laboratories with trained personnel and make available essential antifungal drugs.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTION

Monique Ameyo DORKENOO: Conceptualization (equal); Data curation (equal); Methodology (equal); Validation (equal); Writing-original draft (equal). Akovi Kiki Adjetey-Toglozombio: Writing-original draft (equal); Writing-review & editing (equal). Bright K. Ocansey: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Methodology (equal); Validation (equal); Writing-original draft (equal). Efoe Sossou: Writing-review & editing (supporting). Fiali Lack: Writing-review & editing (supporting). David Denning: Conceptualization (lead); Data curation (equal); Formal analysis (equal); Methodology (lead); Writing-review & editing (supporting).

Ameyo M. Dorkenoo, Bright K. Ocansey and David W. Denning designed the study; Ameyo M. Dorkenoo, Akovi K. Adjetey-Toglozombio, Bright K. Ocansey and David W. Denning collected and analysed the data; Ameyo M. Dorkenoo, Akovi K. Adjetey-Toglozombio and Bright K. Ocansey drafted the manuscript; ES, FL and DD revised the draft. All authors approved the final manuscript.

ORCID

Ameyo M. Dorkenoo https://orcid.org/0000-0002-1030-7757
David W. Denning https://orcid.org/0000-0001-5626-2251

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